

### **REMARKS**

These remarks are in response to the Office Action mailed December 11, 2007.

Applicants respectfully request entry of amendments to claims 1, 2, 3, 6, 10, 12, 19 and 20 and addition of new claims 76-78. Claims 15-18 have been canceled. Subsequent to the entry of the present amendment, claims 1-14 and 19-20 and new claims 76-78 will be pending and at issue.

Applicants submit that the pending claims are in condition for allowance and respectfully request that the amended claims be entered.

#### **I. Amendments**

The claims have been amended to more particularly define the invention. No new matter has been added.

#### **II. Rejection Under 35 U.S.C. §101**

Claims 1-14, 19 and 20 are rejected under 35 U.S.C. §101, allegedly because the disclosed invention is inoperative and lacks utility. Applicants respectfully traverse the rejection as it applies to the pending claims.

Specifically, the Examiner alleges that “claims 1-14, 19, and 20 are inoperative for determining manganese concentration in a cell by measuring reverse transcriptase activity.” The Examiner stated that the “claimed method relies on a spurious assumption that reverse transcriptase activity relies solely on a cell’s ability to transport manganese and maintain a given concentration of manganese within the cell. Lennerstrand et al teach that many anti-reverse transcriptase agent acts by interfering with reverse transcriptase’s ability to elongate the nucleotide chain, i.e., they are incorporated in place of normal nucleotides and prevent further elongation...Based on this mechanism, there is no indication that manganese concentration plays a role in the process.”

Reverse transcriptase is a DNA polymerase enzyme that transcribes single-stranded RNA into single-stranded DNA. Normal transcription involves the synthesis of RNA from DNA; hence, reverse transcription is the reverse of this. It is well known in the art that all nucleic acid

polymerases require a divalent cation, such as magnesium or manganese, as a co-factor for their enzymatic activity. See, for example, the article by Goldschmidt et al (Nuc. Acids Res., 2006), attached hereto as Exhibit A. Even the Lennerstrand et al article cited by the Examiner details the use of magnesium in the reverse transcriptase reaction buffer (p. 2079, right column).

Thus, a divalent cation is a requirement for the enzymatic activity of reverse transcriptase, and thus the concentration of a divalent cation, such as magnesium or manganese, is an important indicator of RT activity as claimed herein. Our work has shown a paradoxical toxic effect of manganese on the activity of magnesium-dependent reverse transcriptase, the present invention for a method of identifying an agent that modulates reverse transcriptase, is operative and a useful invention. Further, Applicants have amended the claims so that manganese concentration is measured and then correlated with an effect on reverse transcriptase activity, rather than directly measuring reverse transcriptase activity. Accordingly, Applicants respectfully request withdrawal of the rejection.

### **III. Rejection Under 35 U.S.C. §112, Second Paragraph**

Claims 1-16 and 18-20 are rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite. Applicants respectfully traverse the rejection as it applies to the pending claims.

Specifically, the Office Action alleges that claim 1 recites “a method of identifying an agent that modulates reverse transcriptase activity in a cell...comprises detecting altered reverse transcriptase activity,” which is allegedly redundant. Applicants respectfully disagrees but notes that the claim has been amended to more clearly define the invention, thereby overcoming the rejection.

Additionally, the Office Action alleges that claim 15 has insufficient antecedent basis. Without acquiescing to the reasoning offered by the Office Action, in order to expedite prosecution toward allowance, Applicants have cancelled claim 15 herein, thereby rendering the rejection moot.

**Rejections under 35 U.S.C. §102**

Claims 1, 3-6, 8-14 and 19 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by Montaner et al., (*J. General Virol.*, 1994, hereafter “Montaner”). Applicants respectfully traverse the rejection as it applies to the claims.

To anticipate, a single reference must inherently or expressly teach each and every element of claimed invention. *In re Spada*, 15 USPQ2d 1655 (Fed Cir. 1990); and *Verdegaal Bros. v. Union Oil Co. of California*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). MPEP § 2131. Furthermore, the reference must be enabling (*see e.g., Chester v. Miller*, 15 U.S.P.Q.2d 1333 (Fed. Cir. 1990)).

Specifically, the Examiner alleges that Montaner teaches a system for studying reverse transcriptase activity in primary macrophages. The Examiner also stated that “claim 17 as written would be interpreted such that any compound inhibiting reverse transcriptase activity would be identified as a manganese transport inhibitor; claim 17 has been incorporated into claim 1 in the Amendment filed 17 September 2007.” While it is true that the claim language of cancelled claim 17 has been incorporated into claim 1, the method of claim 1 contains more language than just the language of canceled claim 17. In its entirety, claim 1 recites a method of identifying agents which modulate the activity of reverse transcriptase, comprising contacting a cell, with a test agent; and detecting elevated intracellular manganese concentrations due to contact with the test agent as compared to intracellular manganese concentrations in the absence of the test agent, wherein detecting elevated manganese levels is an indirect indicator of an inhibition of reverse transcriptase activity. While manganese ion levels are indirectly correlated with reverse transcriptase activity, this goes to the inventive aspect of the invention.

A review of the cited reference indicates that nothing in the reference teaches or suggests a method of identifying an agent which inhibits the activity of reverse transcriptase. Applicants respectfully submit that Montaner fails to teach each and every element of the claimed invention. Montaner does not teach or suggest identifying an agent that inhibits reverse transcriptase activity, therefore the claimed method cannot be enabled by the teachings of Montaner, the cited

reference does not teach or suggest the invention as claimed. Thus, because Montaner fails to teach each and every element of the claimed invention, the standard for anticipation has not been met.

For these reasons, Applicants respectfully request withdrawal of the rejection.

Claims 1-5, 10-14 and 19 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by Simm et al., (*J. Biol. Chem.*, 1996, hereafter “Simm”). Applicants respectfully traverse the rejection as it applies to the claims.

To anticipate, a single reference must inherently or expressly teach each and every element of claimed invention. *In re Spada*, 15 USPQ2d 1655 (Fed Cir. 1990); and *Verdegaal Bros. v. Union Oil Co. of California*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). MPEP § 2131. Furthermore, the reference must be enabling (*see e.g., Chester v. Miller*, 15 U.S.P.Q.2d 1333 (Fed. Cir. 1990)).

Specifically, the Office Action alleges that Simm teaches that “isolated human T-cell membrane vesicles are sufficient to support entry by HIV and reverse transcriptase activity thereafter.” Applicants respectfully submit that Simm fails to teach each and every element of the claimed invention. The present claims recite a method of identifying an agent that inhibits the activity of reverse transcriptase in a cell or cell membrane, and as Simm does not teach or suggest identifying an agent that inhibits reverse transcriptase activity in a cell or cell membrane by specifically measuring intracellular manganese ion levels before and after contact with a test agent, the reference does not teach or suggest the invention as claimed. Thus, because Simm fails to teach each and every element of the claimed invention, the standard for anticipation has not been met.

For these reasons, Applicants respectfully request withdrawal of the rejection.

Claims 1, 3, 4, 6, 7, 10-14 and 20 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by Nissley et al., (*PNAS*, 1998, hereafter “Nissley”). Applicants respectfully traverse the rejection as it applies to the claims.

To anticipate, a single reference must inherently or expressly teach each and every element of claimed invention. *In re Spada*, 15 USPQ2d 1655 (Fed Cir. 1990); and *Verdegaal Bros. v. Union Oil Co. of California*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). MPEP § 2131. Furthermore, the reference must be enabling (*see e.g., Chester v. Miller*, 15 U.S.P.Q.2d 1333 (Fed. Cir. 1990)).

Specifically, the Office Action alleges that Nissley teach an assay for reverse transcriptase activity, and that the assay relies on a hybrid retrotransposon that is composed of yeast Ty1 elements with reverse transcriptase of HIV-1. Applicants respectfully submit that Nissley fails to teach each and every element of the claimed invention. The present claims recite a method of identifying agents which inhibit the activity of reverse transcriptase, and as Nissley does not teach or suggest identifying an agent that inhibits reverse transcriptase activity, nor does it teach measuring intracellular manganese ion levels in the presence and absence of a test agent, the reference does not teach or suggest the invention as claimed. Thus, because Nissley fails to teach each and every element of the claimed invention, the standard for anticipation has not been met.

For these reasons, Applicants respectfully request withdrawal of the rejection.

In re Application of:  
Boeke and Bolton  
Application No.: 10/507,252  
Filed: January 28, 2005  
Page 17

PATENT  
Atty Docket No.: JHU1870-1

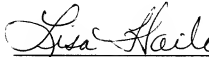
**Conclusion**

Applicants submit that pending claims 1-14, 19-20 and 76-78 are in condition for allowance. The Examiner is invited to contact Applicants' undersigned representative if there are any questions relating to this submission.

No fee is deemed necessary with the filing of this paper. However, the Commissioner is hereby authorized to charge any fees required by this submission, or credit any overpayments, to Deposit Account No. 07-1896 referencing the above-identified docket number.

Respectfully submitted,

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